



Atty. Dkt. No. 071949-5408

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: VALKIRS et al.

Title: DIAGNOSTIC MARKERS OF  
STROKE AND CEREBRAL  
INJURY AND METHODS OF  
USE THEREOF

Appl. No.: 10/714,078

Filing Date: 11/14/2003

Examiner:

Art Unit:

<p><b>CERTIFICATE OF MAILING</b></p> <p>I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450, on the date below.</p> <p><u>DIANE GARCIA</u> (Printed Name)</p> <p><u>Diane Garcia</u> (Signature)</p> <p><u>1-8-2004</u> (Date of Deposit)</p>
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**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Applicants submit herewith on Form PTO/SB/08 a listing of the documents cited by or submitted to the U.S. PTO in corresponding application Serial Nos. 10/371,149, filed 02/20/2003 and 10/225,082, filed 08/20/2002. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent applications.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.



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**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

**RELEVANCE OF EACH DOCUMENT**

All of the documents are in English.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

Respectfully submitted,

Date

1/8/04

By

Barry Wilson

FOLEY & LARDNER

Customer Number: 30542

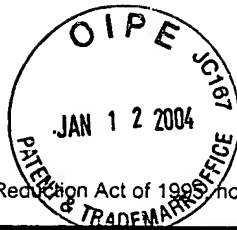
Telephone: (858) 847-6722

Facsimile: (858) 792-6773

Barry S. Wilson

Attorney for Applicant

Registration No. 39,431



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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Substitute for form 1449B/PTO <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		<b>Complete if Known</b>	
		Application Number	10/ 371,149
Sheet 1 of 1		Filing Date	02/20/2002
		First Named Inventor	Gunars E. Valkirs
		Group Art Unit	1632
		Examiner Name	
		Attorney Docket Number	071949-5406

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	A1	6,235,489 B1		Jackowski et al.	May 22, 2001	
	A2	6,268,223 B1		Cornell-Bell et al.	July 31, 2001	

FOREIGN PATENT DOCUMENTS								
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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	A3	WO	00/52476 A1		Skye Pharmatech Incorporated	Sept. 8, 2000		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
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	A4	Feinberg et al., "Guidelines for the Management of Transient Ischemic Attacks." Stroke, 25(6): 1320-1335, June 1994.	
	A5	Herrmann et al., "Release of Glial tissue-specific proteins after acute stroke: A comparison analysis of serum concentrations of protein S-100B and Glial fibrillary acidic protein." Stroke, 31:2670-2677, 2000.	
	A6	Napoli et al., "C-reactive protein in ischemic stroke: An independent prognostic factor." Stroke, 32:917-924, 2001.	
	A7	Strand et al., "Brain and plasma proteins in spinal fluid as markers for brain damage and severity of stroke." Stroke, 15(1): 138-144, 1994.	
	A8	Hirashima et al., "Elevation of platelet activating factor, inflammatory cytokines, and coagulation factors in the internal jugular vein of patients with subarachnoid hemorrhage." Neurochemical Research, 22(10): 1249-1255, 1997.	

Examiner Signature		Date Considered	
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Sheet	2	of	1

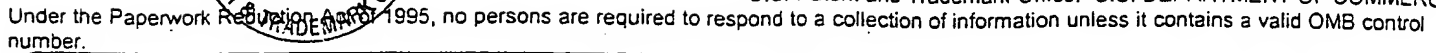
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Application Number	10/225,082
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First Named Inventor	Gunars E. Valkirs
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Attorney Docket Number	071949-5404

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		First Named Inventor	Gunars E. Valkirs
		Group Art Unit	1632
		Examiner Name	
Sheet	2	of	21
		Attorney Docket Number	071949-5404

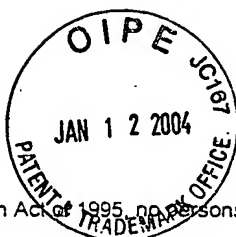
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	A20	Akiyama et al., "Changes in serum concentrations of matrix metalloproteins, tissue inhibitors of metalloproteinases and Type IV collagen in patients with various types of glomerulonephritis," Res. Commun. In Mol. Path. and Pharm., 95(2): 115-128, 1997.	
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	A22	Albrechtsen and Bock, "Quantification of glial fibrillary acidic protein (GFAP) in human body fluids by means of ELISA employing a monoclonal antibody." Journal of Neuroimmunology, 8:301-309, 1985.	
	A23	Austgulen et al., "Increased maternal plasma levels of soluble adhesion molecules (ICAM-1, VCAM-1, E-selectin) in preeclampsia," Eur. J. Obstet. Gynecol. Reprod. Biol., 71:53-58, 1997.	
	A24	Banks et al., "Circulating intercellular adhesion molecule-1 (ICAM-1), E-selectin and vascular cell adhesion molecule-1 (VCAM-1) in human malignancies," Br. J. Cancer, 68:122-124, 1993.	
	A25	Bates et al., "Neurotrophin-3 promotes cell death induced in cerebral ischemia, oxygen-glucose deprivation, and oxidative stress: possible involvement of oxygen free radicals," Neurobiology of Disease, :24-37, 2002.	
	A26	Benamer et al., "Comparison of the prognostic value of C-reactive protein and troponin I in patients with unstable angina pectoris," Am. J. Cardiol., 82:845-850, 1998.	
	A27	Berendes et al., "Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid haemorrhage," Lancet, 349:245-249, 1997.	
	A28	Bialik et al., "Myocyte apoptosis during acute myocardial infarction in the mouse localizes to hypoxic regions but occurs independently of p53," J.Clin.Invest., 100(6): 1363-1372, 1997.	
	A29	Biasucci et al., "Elevated levels of interleukin-6 in unstable angina," Circulation, 94:874-877, 1996.	
	A30	Biasucci et al., "Episodic activation of the coagulation system in unstable angina does not elicit an acute phase reaction," Am. J. of Cardiol., 77:85-87, 1996.	

Examiner Signature	Date Considered
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STATEMENT BY APPLICANT

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Sheet 3 of 21

Complete if Known

Application Number	10/225,082
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First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
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	A31	Biasucci et al., "Increasing levels of interleukin (IL)-1Ra and IL-6 during the first 2 days of hospitalization in unstable angina are associated with increased risk of in-hospital coronary events," Circulation, 99:2079-2084, 1999.	
	A32	Bitsch et al., "A longitudinal prospective study of soluble adhesion molecules in acute stroke," Stroke, 29:2129-2135, 1998.	
	A33	Blankaert et al., "Constitutive release of metalloproteinase-9 (92-kd Type IV collagenase) by Kaposi's sarcoma cells," J. Acquir. Immune Defic. Syndr. Hum. Retrovir., 18:203-209, 1998.	
	A34	Blann et al., "Soluble intercellular adhesion molecule-1, E-selectin, vascular cell adhesion molecule-1 and von Willebrand factor in stroke," Blood Coagul. Fibrinolysis, 10:277-284, 1999.	
	A35	Bollensen et al., "Adenylate kinase enzyme activity in cases of brain infarction," Acta Neurol. Scand., 79:53-58, 1989.	
	A36	Bonfrer et al., "The luminescence immunoassay S-100: a sensitive test to measure circulating S-100B: its prognostic value in malignant melanoma," Brit. Jour. Of Cancer, 77(12): 2210-2214, 1998.	
	A37	Bonow, "New insights into the cardiac natriuretic peptides," Circulation, 93:1946-1950, 1996.	
	A38	Bossink et al., "Plasma levels of the chemokines monocyte chemotactic proteins-1 and -2 are elevated in human sepsis," Blood, 86(10): 3841-3847, 1995.	

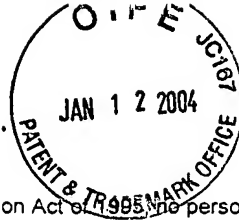
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		Filing Date	08/20/2002
		First Named Inventor	Gunars E. Valkirs
		Group Art Unit	1632
		Examiner Name	
Sheet	4	of	21
		Attorney Docket Number	071949-5404

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
	A39	Caligiuri et al., "Immune system activation follows inflammation in unstable angina: pathogenetic implications," J.Am. Coll. Cardiol., 32:1295-1304, 1998.	
	A40	Carlstedt et al., "Proinflammatory cytokines, measured in a mixed population on arrival in the emergency department, are related to mortality and severity of disease," Journal of Internal Medicine, 242:361-365, 1997.	
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	A42	Carter et al., "Purification, cloning, expression and biological characterization of an interleukin-1 receptor antagonist protein," Nature, 344:633-638, 1990.	
	A43	Catto et al., "von Willebrand factor and factor VIII: C in acute cerebrovascular disease," Thromb. Haemost., 77:1104-8, 1997.	
	A44	Curzen et al., "Can C reactive protein or troponins T and I predict outcome in patients with intractable unstable angina?" Heart, 80:23-27, 1998.	
	A45	Dangas et al., "Correlation of serum lipoprotein(a) with the angiographic and clinical presentation of coronary artery disease," Am. J. Cardiol., 83:583-585, 1999.	
	A46	Davie et al., "The coagulation cascade: initiation, maintenance and regulation," Biochemistry, 30(43): 10363-10370, 1991.	

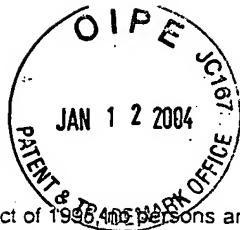
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	A47	DeRose et al., "Circulating adhesion molecules in cystic fibrosis," Am. J. Respir. Crit. Care Med., 157: 1234-1239, 1998.	
	A48	Eisenberg et al., "Interleukin 1 receptor antagonist is a member of the interleukin 1 gene family: evolution of a cytokine control mechanism," Proc. Nat. Acad. Sci. USA, 88: 5232-5236, 1991.	
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	A50	Endo et al., "Elevated levels of serum and plasma metalloproteinases in patients with gastric cancer," Anticancer Research, 17:2253-2258, 1997.	
	A51	Estrada et al., "High plasma levels of endothelin-1 and atrial natriuretic peptide in patients with acute ischemic stroke," Am. J. of Hypertension, 7(12): 1085-1089, 1994.	
	A52	Fassbender et al., "Proinflammatory cytokines in serum of patients with acute cerebral ischemia: kinetics of secretion and relation to the extent of brain damage and outcome of disease," Journal of the Neurological Sciences, 122:135-139, 1994.	
	A53	Feinberg et al., "Hemostatic markers in acute ischemic stroke," Stroke, 27:1296-1300, 1996.	
	A54	Fernandes-Alnemri et al., "CPP32, a novel human apoptotic protein with homology to <i>Caenorhabditis elegans</i> cell death protein Ced-3 and mammalian interleukin-1 $\beta$ -converting enzyme," Journal of Biological Chemistry, 269(49): 30761-30764, 1994.	

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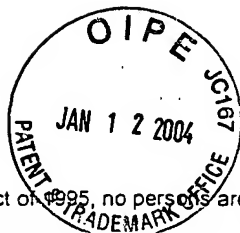
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	A55	Fisher et al., "Serum concentrations and peripheral secretion of the beta chemokines monocyte chemoattractant protein 1 and macrophage inflammatory protein 1 $\alpha$ in alcoholic liver disease," Gut, 45(3): 416-420, 1999.	
	A56	Fon et al., "Hemostatic markers in acute transient ischemic attacks," Stroke, 25(2): 282-286, 1994.	
	A57	Fujii et al., "Hemostasis in spontaneous subarachnoid hemorrhage," Neurosurgery, 37(2): 226-234, 1995.	
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		Application Number	10/225,082
		Filing Date	08/20/2002
		First Named Inventor	Gunars E. Valkirs
		Group Art Unit	1632
		Examiner Name	
Sheet	7	of	21
		Attorney Docket Number	071949-5404

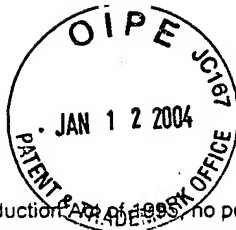
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Sheet 9 of 21

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Filing Date	08/20/2002
First Named Inventor	Gunars E. Valkirs
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First Named Inventor	Gunars E. Valkirs
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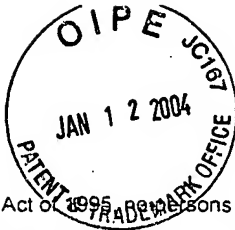
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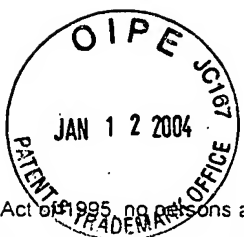
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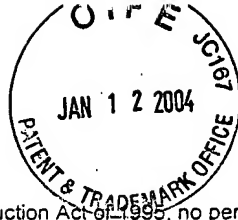
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	A118	Mun-Bryce and Rosenberg, "Matrix metalloproteinases in cerebrovascular disease," J.Cereb. Blood Flow Metab., 18:1163-1172, 1998.	

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Sheet 14 of 21

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Application Number	10/225,082
Filing Date	08/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	
Attorney Docket Number	071949-5404

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>5</sup>
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	A120	Nishiyama et al., "Simultaneous elevation of the levels of circulating monocyte chemoattractant protein-1 and tissue factor in acute coronary syndromes," Jpn. Circ. J., 62:710-712, 1998.	
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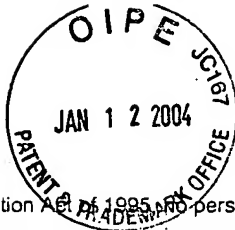
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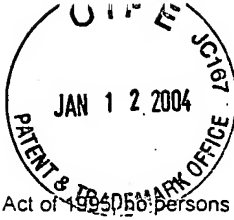
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		Filing Date	08/20/2002
		First Named Inventor	Gunars E. Valkirs
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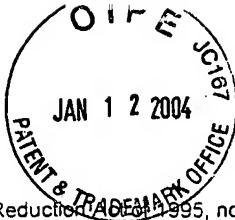
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	A141	Seki et al., "Sustained activation of blood coagulation in patients with cerebral thrombosis," A. J. Hematol., 50: 155-160, 1995.	
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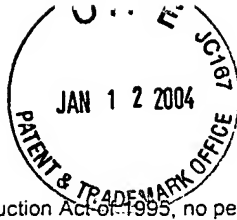
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		Group Art Unit	1632
		Examiner Name	
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		Attorney Docket Number	071949-5404

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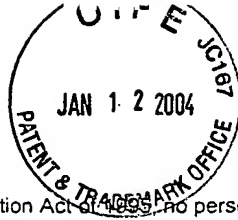
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	A151	Sviri et al., "Brain natriuretic peptide and cerebral vasospasm in subarachnoid hemorrhage: Clinical and TCD correlations," Stroke, 31:118-122, 2000.	
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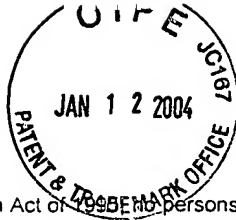
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	A160	Tousoulis et al., "Von Willebrand factor in patients evolving Q-wave versus non-Q-wave acute myocardial infarction," Int. J. Cardiol., 56:259-262, 1996.	
	A161	Trotter et al., "Immunoreactive myelin proteolipid protein-like activity in cerebrospinal fluid and serum of neurologically impaired patients," Ann. Neurol., 14: 554-558, 1983.	
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	A167	Wilkins et al., "The natriuretic-peptide family," Lancet, 349:1307-1310, 1997.	
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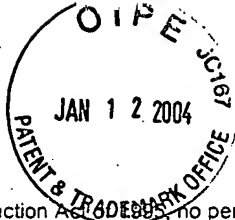
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		Application Number	10/225,082
		Filing Date	08/20/2002
		First Named Inventor	Gunars E. Valkirs
		Group Art Unit	1632
		Examiner Name	
Sheet	21	of	21
		Attorney Docket Number	071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
	A175	Yoneda et al., "Identification of a novel adenylate kinase system in the brain: Cloning of the fourth adenylate kinase," Mol. Brain Res., 62: 187-195, 1998.	
	A176	Yoshimura et al., "Human monocyte chemoattractant protein-1 (MCP-1)," FEBS Lett., 244:487-493, 1989.	
	A177	Yoshitomi et al., "Plasma levels of adrenomedullin in patients with acute myocardial infarction," Clin. Sci. 94:135-9, 1998	
	A178	Zucker et al., "Increased serum stromelysin-1 levels in systemic lupus erythematosus: lack of correlation with disease activity," J.Rheumatol., 26:78-80, 1999.	

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